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## Presentation Abstract

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Presentation Title: Direct hippocampal-prefrontal input supports the encoding of spatial information during a working memory task

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**Abstract:** Spatial working memory in rodents requires an intact hippocampus (HPC) and medial prefrontal cortex (mPFC), and synchrony between these structures is modulated by working memory demand. Pyramidal cells of intermediate and ventral CA1 and subiculum send direct glutamatergic projections to the mPFC, but the functional role of that direct input in behavior and synchrony is unknown. To study this role, we utilized the light-driven proton pump eArch3.0 to inhibit HPC-mPFC afferents in a temporally-precise and reversible manner during a T-maze delayed non-match to place task. Following T-maze training, HPC-mPFC terminal fields were inhibited during a subset of interleaved, pseudo-randomized trials in one of four task phases: All Off (no light), All On (light during the entire trial), Sample On (light during sample run/encoding), or Choice On (light during choice run/retrieval). In eArch3.0-expressing animals, but not in opsin-negative controls, T-Maze performance was significantly impaired during All On and Sample On trials, but not Choice On trials ( $p = 0.002$  and  $p = 0.003$ , respectively). To further define the functional role of the direct input, we used a novel 4-goal variant of the task to temporally segregate encoding and retrieval, and conducted simultaneous paired extracellular recordings from vHPC and mPFC during task performance. Inhibiting during the encoding but not retrieval phase impaired performance ( $t = 3.1$ ,  $p = 0.0097$ ). Single units in the mPFC phase-locked to the prominent 30-70Hz gamma

oscillation of the vHPC in a task-related manner, such that phase locking was higher during encoding than during retrieval, and higher on correct than incorrect trials (sign rank,  $p = 0.0001$  and  $p = 0.001$ , respectively). This synchrony was disrupted during terminal field illumination in eArch-treated but not control mice (sign rank,  $p = 0.0006$  and  $p = 0.19$ , respectively). Finally, using a maximum margin linear classifier, we found that sample goal location could be robustly decoded from mPFC spike trains, and that this representation was disrupted during HPC-mPFC terminal inhibition. These results suggest a specific role for the direct HPC-mPFC input for encoding, though not maintenance or retrieval, of working memory-related spatial information.

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